

# Modeling the Cost of Management Options for small benign non-functional adrenal incidentaloma: A Decision Tree Analysis

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## Research article

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# Abstract

**Objective** Using decision analysis to determine the economic benefits of surgery versus surveillance for patients with small benign non-functional adrenal incidentaloma. **Methods** A detailed model was developed that integrates projected costs for a few possible treatment outcomes. Starting values and probabilities were derived from a comprehensive meta-analysis of 1298 patients. Hypothesis testing was performed using sensitivity analysis. **Results** The model predicts a cost premium for follow-up compared with surgery. The tornado analysis identifies the cost of follow-up for once as the most important variables for our model. One-way sensitivity analysis demonstrated that cost equivalence could be met with ¥4359.5 for once follow-up, keeping other factors constant. **Conclusion** Our models of treatment for small benign non-functional adrenal incidentaloma showed significant cost differences for follow-up versus immediate surgery. The cost of follow-up for once featured threshold values.

## Introduction

Adrenal incidentaloma (AI) is the term for any unsuspected lesion of the adrenal gland found by radiological imaging, usually done for other indications. Since AI is a clinical dilemma, several organizations including the National Institutes of Health (NIH), the European Society of Endocrinology<sup>1</sup> (ESE) and the European Network for the Study of Adrenal Tumors (ENSAT) published guidelines to improve the evaluation and management of these patients. Although it is consistently recommended that hyper-functional tumor and suspicious malignancy need surgery, the management of patients with small benign non-functional adrenal incidentaloma remains controversial and some experts recommend surgery rather than surveillance<sup>2-4</sup>. Contrast to temporary guidelines, in our previous report<sup>5</sup>, silent malignancy and pheochromocytoma were not rare; also some studies demonstrated that follow-up was associated with a higher incidence of metabolic syndrome<sup>6</sup>. As small benign non-functional adrenal incidentaloma within initial assessment may progress to hyper-functional, larger size or malignancy plus anxiety is burdensome for some patients, both in economic and psychology, surgery could be another choice besides surveillance.

Here we develop a detailed mathematical decision analysis model comparing the projected management costs for small benign non-functional adrenal incidentaloma. It is built on a meta-analysis<sup>7</sup> and reflects a multi-institutional clinical experience. The model incorporates a variety of clinical outcomes downstream from the original clinical decision (Figure 1), given that these events would potentially influence costs.

## Methods

Decision analytic models are methods of estimating and calculating outcomes by identifying the clinical question, disaggregating the problem into discrete units to include all reasonable choices and consequences, and assigning probabilities and value to the various events and outcomes. The decision model was designed and analyzed using TreeAge Pro software with the Healthcare suite (available

<http://www.treeage.com>). Surveillance versus surgery of small benign non-functional adrenal incidentaloma constituted the arms of the decision tree (Figure 1).

## Model assumptions

According meta-analysis from Loh HH<sup>7</sup>, we assume 1.5% of cases end up surgery for developing Cushing's syndrome or pheochromocytoma at the third year of follow-up, and the same percentage of cases accept surgeries at the fourth year. The rest of others complete the five-year follow-up without surgery.

## Costs, charges, and time values

The surgeon's fee and anesthesiologist's fee, as well as the charges of pre-operation stay, post-operation stay and follow-up, were all derived from Zhuhai Peoples' hospital of Guangdong province in China in 2018. (Table 1)

The costs for each treatment arm were calculated as the average costs for all patients in each arm and were cumulative from the beginning until the end of follow-up or surgery. The annual inflation rate is not constant, we incorporate the approximate average number, 5%, into the cost.

## Sensitivity analysis

To address the effect of the individual variables on our model and test the validity of our model assumptions, we performed 1-way sensitivity analysis on all model parameters. This was performed by individually varying each variable for a range of values, keeping all other variables constant. If the resulting costs were unchanged, the analysis was considered "insensitive" to the tested variable. Otherwise, we calculated the threshold (ie, "crossover point") at which a given value for the variable in question would change which treatment arm featured the lowest overall costs.

The variables that featured threshold values on 1-way analysis were also used for 2-way sensitivity analysis, in which 2 variables were varied simultaneously, and the thresholds were measured.

## Results

### Base-case analysis

The base case analysis demonstrated follow-up featured the lowest overall cost per patient (¥7213) compared with immediate surgery (¥24691)(Figure 2).

### Sensitivity analysis

The tornado analysis, which included 1-way sensitivity analysis of all parameters, was used to identify the most important variables for our model. The cost of follow-up for once was the most important because varying this parameter during the sensitivity analysis resulted in the greatest effects on costs (wider bars in the tornado diagram); other values that had a minimal effect on the analysis(Figure 3).

To identify the cost of follow-up for once resulting in cost equivalence between follow-up and immediate surgery, we performed a one-way sensitivity analysis. This analysis demonstrated that cost equivalence could be met with ¥4359.5 for once follow-up, keeping other factors constant(Figure 4).

Because the cost of follow-up for once was the only parameter demonstrating threshold value, we focused the 2-way sensitivity analysis on this set of parameters. Using two-way sensitivity analysis, cost of follow-up for once and length of post-surgery stay were varied to evaluate how these factors affected the choice of the least costly therapy option. For the majority of the cost of follow-up for once and length of post-surgery stay, the follow-up shows a clear cost advantage(Figure 5).

## Discussion

When facing small benign non-functional adrenal incidentaloma, patients and urologists must decide between follow-up and surgery. This decision hinges on the critical issues of effectiveness, morbidity and cost. Both options have good outcomes. Only Belmihoub<sup>8</sup> reported one case that benign adrenal incidentaloma progressed adrenocortical carcinoma. Loh HH<sup>7</sup> reported that no surgery is done due to primary adrenal malignancy during follow-up. Likewise, the morbidity of surgery is mild<sup>9-12</sup>. Cost may, therefore, play an important role in directing clinical decisions in this disease. A detailed decision-tree model was developed for projecting the management costs for small benign non-functional adrenal incidentaloma. The model's advantage lies in the ease with which various hypotheses can be rapidly tested through the use of sensitivity analysis.

The current model includes treatment-related morbidity because the various cost derived from the actual charge from patients and/or medical insurance bureau. Three of 21 patients had surgery complication, which is similar to other reports<sup>9-12</sup>. One patient complicated major hemorrhage and transferred to open surgery, another one had urinary infection and fever, the third one had pneumonia after surgery. Although these three patients stayed longer than the average length of stay and cost more than the others, they were discharged with good health finally.

As a model based on temporary data, limitations are inevitable. The mortality difference between surveillance and immediate surgery is seemed to be minor, and the use of mortality as a measure of effectiveness is unavailable. Estimates based on such small and controversial differences in morbidity would mistake the results. And cost modeling is correlated with local environment, and utility of this model should be adjusted to other centers provided that institution-specific cost components are modified. Finally, because we examined the costs from the perspective of the medical establishment,

indirect costs, such as psychological factor, were not included. No published work is available regarding the indirect costs of surveillance versus immediate surgery. This is an area worthy of additional study.

## Conclusions

Our models about the management of small benign non-functional adrenal incidentaloma showed significant cost differences for follow-up vs immediate surgery. The cost of follow-up for once featured threshold values.

## Declarations

## Competing interests

The authors declare that they have no competing interests.

## Ethics approval and consent to participate

Due to the retrospective nature of this study, ethics approval by our Institutional Review Board was obtained and the data were used confidentially for research work. Informed consent was obtained by every patient when they referred to the hospital.

## Declaration

The dataset supporting the conclusions of this article is included within the article and its additional files.

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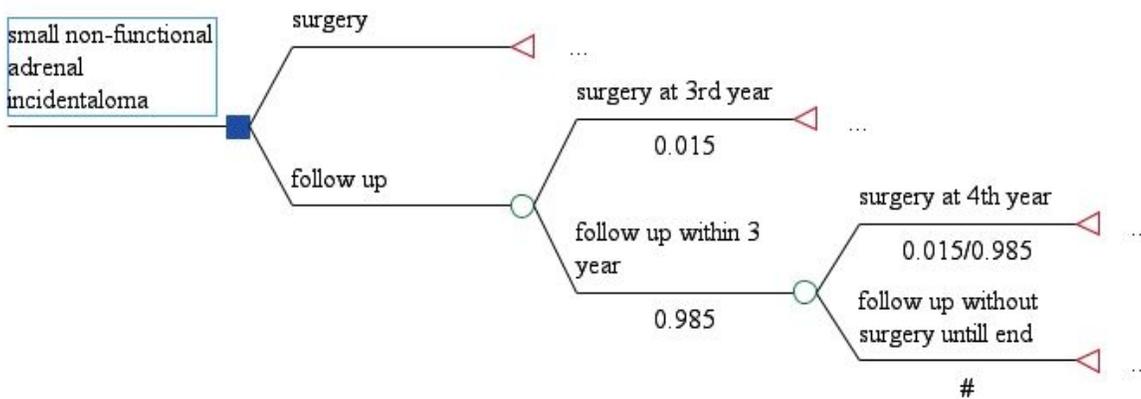
## Table

Table 1: cost and charge of each patient

PID	TC	LOS	DC	PreSC	LOPreSS	DCBS	AF	SF	PostSC	LOPostSS	DCAS	TOS
485468	22712.2	11	2064.7	7092.2	6	1182.0	4836.2	8721.9	2061.9	5	412.4	110
490273	47748.9	16	2984.3	6848.3	5	1369.7	10507.3	9889.5	20503.8	11	1864.0	265
454471	31107.3	21	1481.3	11695.8	14	835.4	5048.0	10284.5	4079.0	7	582.7	185
488745	26848.4	26	1032.6	11165.8	19	587.7	3063.2	7841.4	4778.1	7	682.6	115
433868	29440.7	20	1472.0	8751.1	10	875.1	4503.5	8781.7	7404.4	10	740.4	255
484723	33960.3	14	2425.7	10129.9	5	2026.0	3456.3	9842.4	10531.8	9	1170.2	135
493007	18755.3	8	2344.4	6309.3	4	1577.3	2904.2	7982.6	1559.2	4	389.8	90
493110	25618.5	11	2329.0	7979.7	5	1595.9	3079.6	9865.4	4693.8	6	782.3	240
493721	20803.7	18	1155.8	9015.6	15	601.0	3289.5	6164.9	2333.7	3	777.9	120
491777	21885.4	14	1563.2	5757.8	9	639.8	2866.7	8185.4	5075.6	5	1015.1	120
491791	24055.5	10	2405.6	7515.3	5	1503.1	4030.4	9435.1	3074.7	5	614.9	135
491770	29463.2	10	2946.3	9714.9	3	3238.3	3471.9	9385.4	6891.0	7	984.4	145
453794	23038.6	11	2094.4	5694.9	6	949.2	4516.8	9321.4	3505.5	5	701.1	110
495208	22424.9	10	2242.5	7859.3	5	1571.9	2590.4	8185.4	3789.9	5	758.0	120
350331	23169.5	13	1782.3	8085.7	8	1010.7	3953.9	8710.1	2419.8	5	484.0	300
335045	20997.9	9	2333.1	5309.6	4	1327.4	2585.2	9345.4	3757.7	5	751.5	130
491232	25399.1	13	1953.8	12666.1	8	1583.3	2662.5	8453.9	1616.7	5	323.3	256
478221	21475.1	9	2386.1	5278.4	4	1319.6	3006.7	9821.6	3368.5	5	673.7	110
497285	20564.4	11	1869.5	6913.5	7	987.6	3206.2	8713.9	1730.8	4	432.7	145
494903	23263.7	10	2326.4	8873.5	6	1478.9	3006.5	9345.4	2038.3	4	509.6	120
498139	21571.2	11	1961.0	3328.6	3	1109.5	3393.5	8673.9	6175.2	8	771.9	80
393877	24408.7	11	2219.0	6807.0	6	1134.5	3549.0	10170.4	3882.3	5	776.5	145
322924	21557.2	10	2155.7	5854.5	5	1170.9	2398.2	9833.4	3471.2	5	694.2	95
477631	34762.2	10	3476.2	8842.4	3	2947.5	5087.0	9445.4	11387.5	7	1626.8	255
499334	31729.9	18	1762.8	7410.6	6	1235.1	4906.3	11006.4	8406.6	12	700.6	230
501786	22406.2	9	2489.6	7917.6	4	1979.4	3836.2	7596.4	3056.0	5	611.2	145
501960	23369.9	14	1669.3	8412.1	9	934.7	5055.9	7019.7	2882.2	5	576.4	125
497189	25976.5	11	2361.5	10443.5	5	2088.7	3294.4	9394.1	2844.5	6	474.1	135
482067	23366.3	11	2124.2	7904.8	8	988.1	4657.9	9270.1	1533.5	3	511.2	135
504594	29434.7	20	1471.7	10011.5	6	1668.6	4321.1	8113.1	6989.0	14	499.2	195
507882	21273.9	12	1772.8	7704.4	8	963.0	3704.4	7570.4	2294.8	4	573.7	155
508619	22370.2	14	1597.9	10125.4	10	1012.5	2727.7	7419.6	2097.4	4	524.4	115
458474	20939.3	11	1903.6	6488.4	4	1622.1	3210.3	7249.7	3991.0	7	570.1	120
506979	34178.0	11	3107.1	16712.4	7	2387.5	5769.1	8243.1	3453.3	4	863.3	105

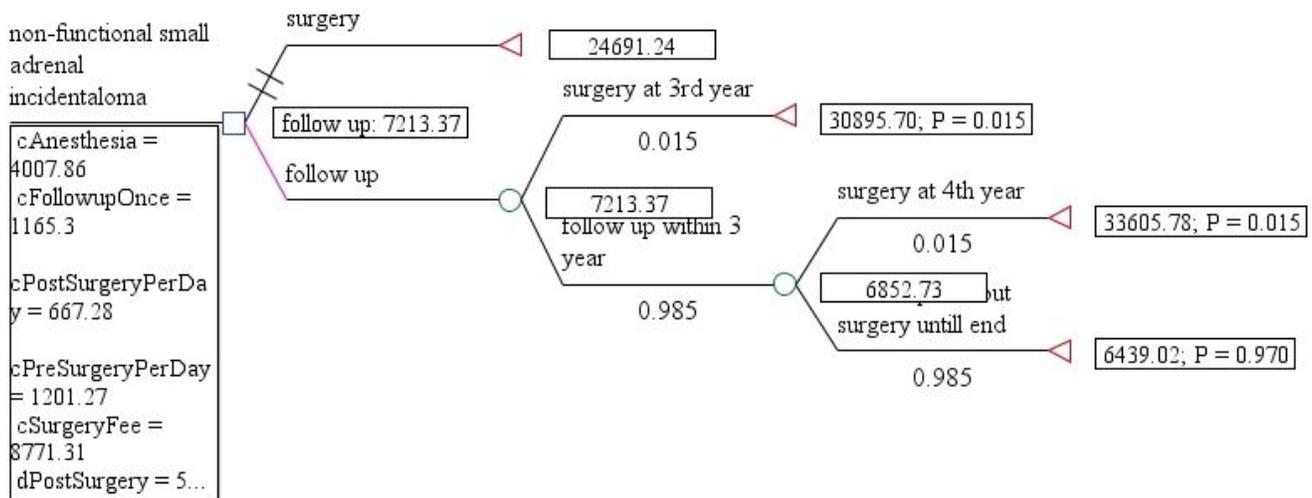
Abbreviation: PID, patient ID; TC, total cost; LOS, length of stay; DC, daily cost; PreSC, pre-surgery cost; LOPreSS, length of pre-surgery stay; DCBS, length of pre-surgery stay; AF, anesthesia fee; SF, surgery fee; PostSC, post-surgery cost; LOPostSS, length of post-surgery stay; DCAS, daily cost after surgery; TOS, time of surgery

# Figures



**Figure 1**

Basic diagram of the decision tree model for the cost of treatment options for small benign non-functional adrenal incidentaloma



**Figure 2**

Comparison of costs of 2 options Sensitivity Analysis

### Tornado Sensitivity Analysis

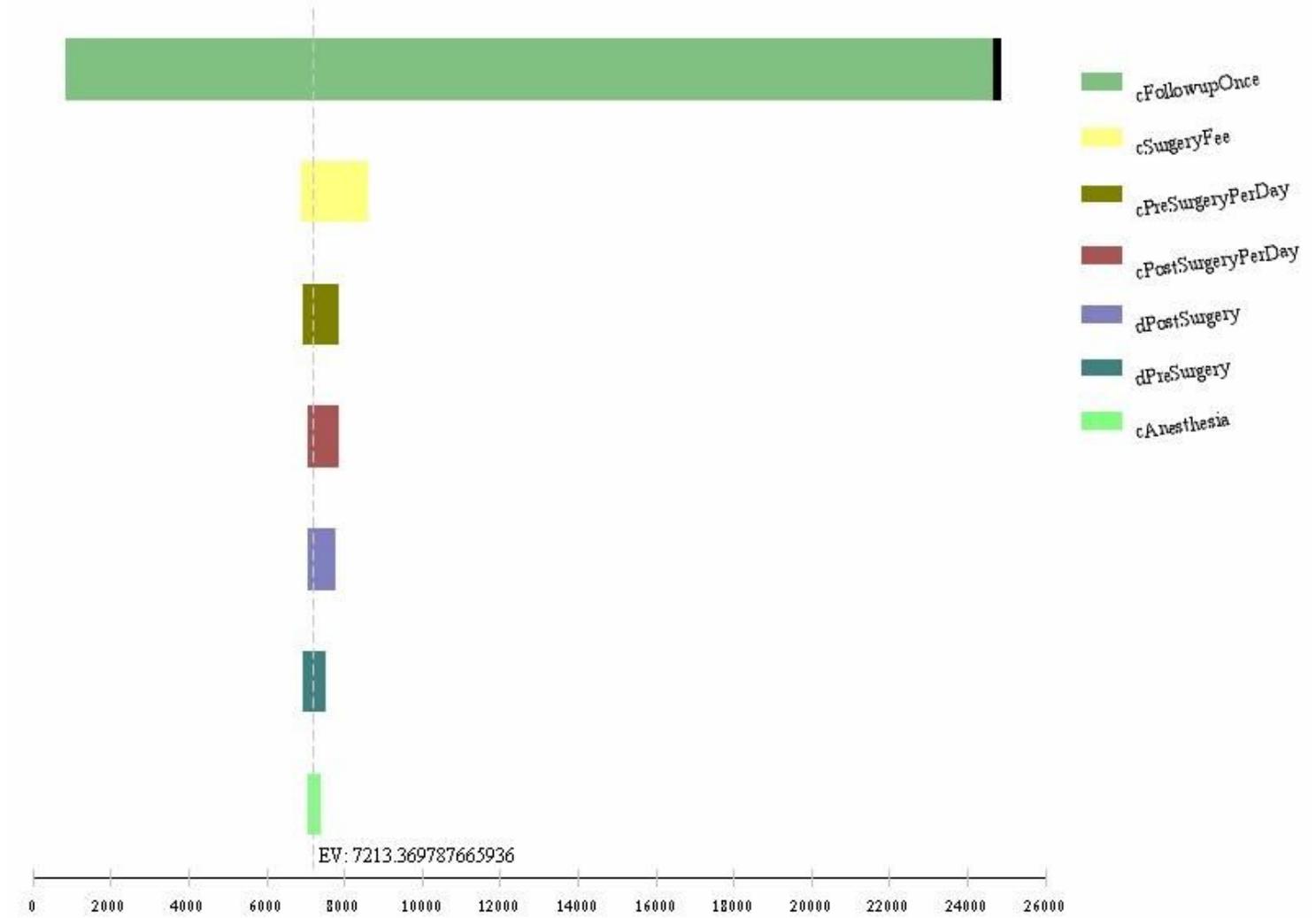


Figure 3

Tornado sensitivity analysis of our model

## Sensitivity Analysis

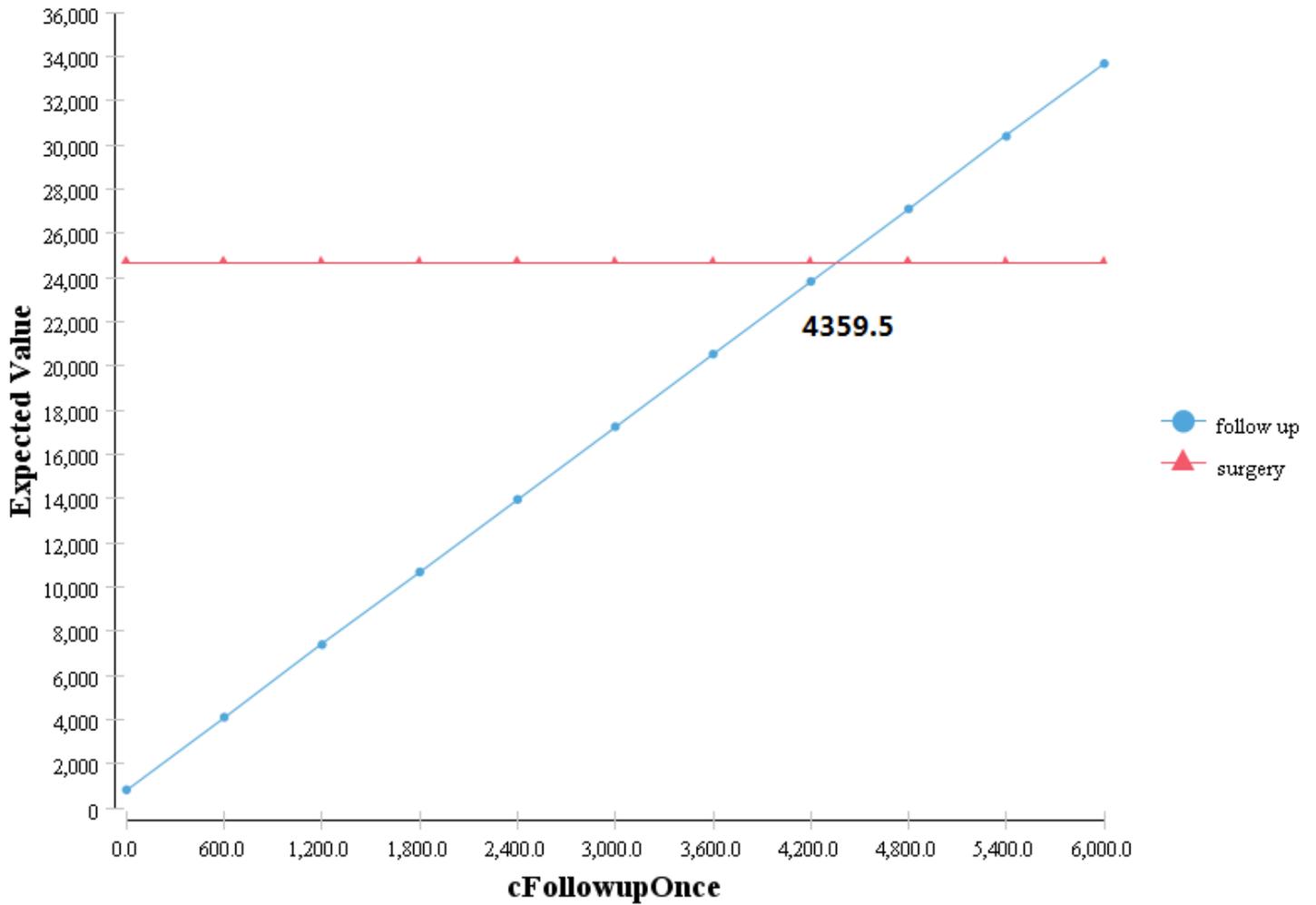


Figure 4

Equivalence point of cost of follow-up for once(x-axis: cost of follow-up for once, y-axis: expected value of 2 options; ¥4359.5 for once follow-up make 2 options equivalent)

## two-way Sensitivity Analysis on dPostSurgery and cFollowupOnce

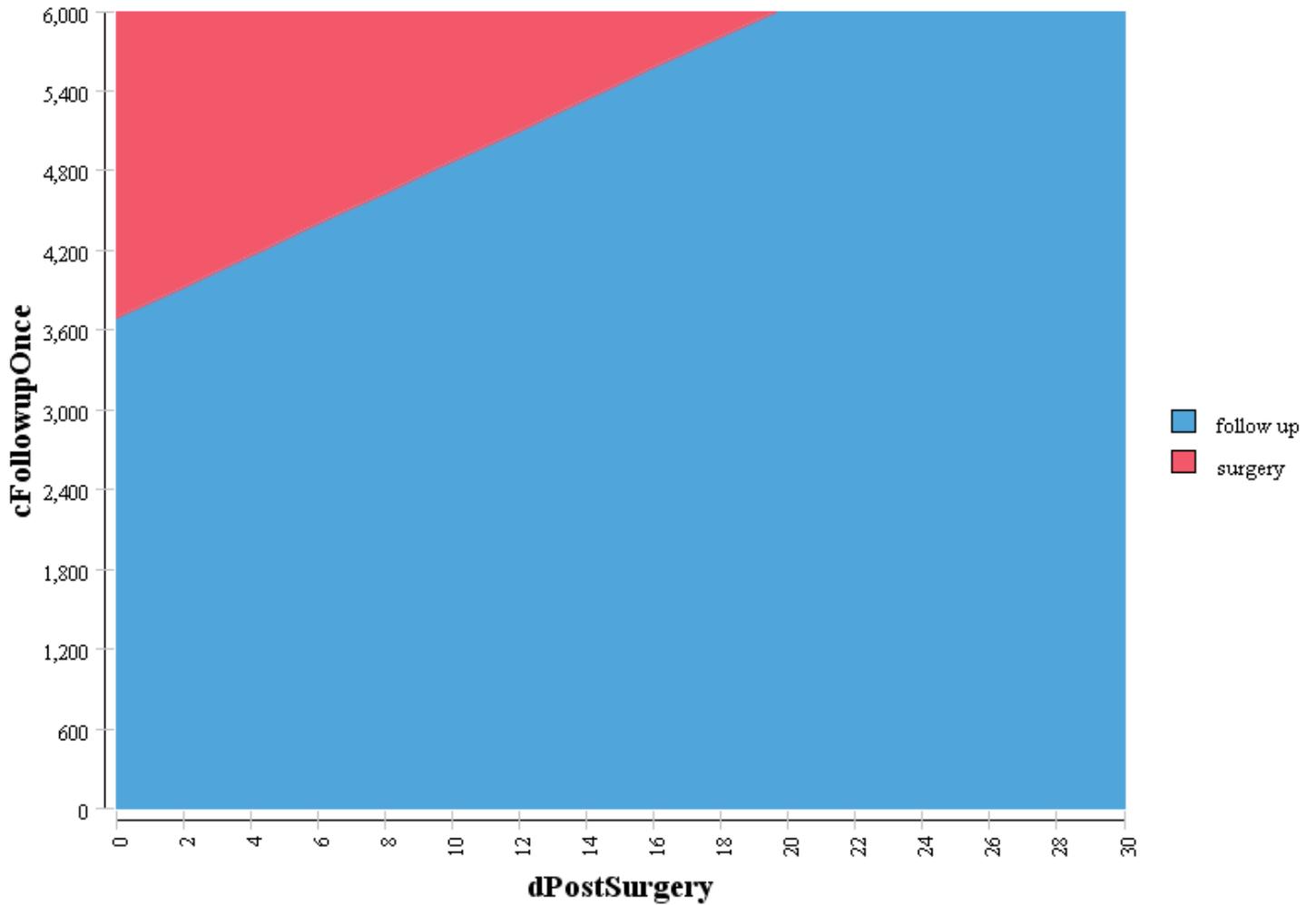


Figure 5

Two-way sensitivity analysis on the cost of follow-up for once and length of post-surgery stay(x-axis: length of stay after surgery, y-axis: cost of follow-up for once; blue area: follow-up cost less, red area: surgery cost less)